for the development of a post transplant cardiac complication. In patients who suffered a cardiac complication 38% went onto require intensive supportive care and this was associated with significant morbidity. Consideration to add medical prophylaxis in patients with a risk to develop cardiac complications should be considered in this high risk group.

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PALIFERMIN REDUCES THE INCIDENCE OF ORAL MUCOSITIS AFTER ABLATIVE PREPARATIVE REGIMENS IN PATIENTS UNDERGOING AN UMBILICAL CORD BLOOD TRANSPLANT

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Oral mucositis (OM) is a major cause of morbidity after myeloablative stem cell transplants. Palifermin has shown efficacy in the prevention of myeloablative therapy-induced OM in patients undergoing autotransplants for hematologic malignancies. We analyzed data from recipients of umbilical cord blood transplantation (UCBT) who received palifermin as prophylaxis for OM both before and after an ablative preparative regimen. **Methods:** We identified 26 UCBT patients at our institution who underwent the procedure from May 2003 to August 2006. The first 15 patients did not receive palifermin while the most recent 11 patients received palifermin at a mean total dose of 150 μg/kg over 2 consecutive days, starting 2 days before the initiation of the preparative regimen and 2 days after infusion of the UCB cells starting on day 0. Patient Characteristics: The median age for the patients in the palifermin vs. non-palifermin groups was 50 (33-58) and 43 (23-56) years. The preparative regimens used for the palifermin group consisted of total body irradiation and cyclophosphamide (TBI/Cy) in 9/11 patients, and BCNU, etoposide, cytarabine and melphalan (BEAM) in 2/11 patients, while in the non-palifermin group, TBI/CY was used in 7/15 patients, BEAM in 5/15 patients, and 2/15 patients received busulfan and cyclophosphamide. The median post-thaw nucleated cell dose for the palifermin vs. non-palifermin groups was 1.4 and 1.7 $\times$ 10^7/kg. **Results:** Mucositis occurred less frequently (2/11 vs. 12/15; *$P = 0.004$, Fisher's exact test*) and appeared to be less severe in the palifermin treated group who also did not have a higher incidence of severe acute graft vs. host disease. No difference was observed in neutrophil (19 vs. 16 days for palifermin vs. non-palifermin) and platelet engraftment (57 and 51 days respectively) between the groups. Days of fevers were less frequent in the palifermin group compared to the non-palifermin group (median of 1 day vs. 4 days respectively). Median days of total parenteral nutrition (TPN) was 0 in the palifermin group vs. 13 days in the non-palifermin group. **Conclusion:** Palifermin reduces the incidence of OM and the need for TPN but does not appear to increase the incidence of severe acute GVHD in recipients of UCBT transplants after myeloablative therapy.

Grade of Mucositis and Acute GVHD With or Without Palifermin in Umbilical Cord Blood Transplant Patients.

Treatment Group	No.	Mucositis Grade 0	Mucositis Grade 1-2	Mucositis Grade 3-4	GVHD Grade 0-I	GVHD Grade II-IV	GVHD Grade III-IV
Palifermin	11	9	1	1	10	1	1
Non-Palifermin	15	3	9	3	3	7	2

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AMD 3100 SUCCESSFULLY MOBILIZES AUTOLOGOUS CD34+ CELLS AFTER FAILURE OF G-CSF MOBILIZATION REGIMENS WITH LOW TOXICITY AND ACCEPTABLE AUTOLOGOUS STEM CELL TRANSPLANT (ASCT) OUTCOMES

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AMD3100 reversibly inhibits SDF-1alpha/CXCR4 binding and induces rapid mobilization of CD34+ cells into the circulation which can potentiate stem cell mobilization by G-CSF alone. We report our institutional experience using AMD3100, as part of a larger compassionate use protocol, in patients (pts) who failed to collect 2 million CD34+ cells/kg using standard methods of autologous peripheral blood stem cell mobilization (PBSCM). Twelve pts (male n=6, median age 65 years [range 32-73]) with non Hodgkins lymphoma (n=6), multiple myeloma (n=4), and Hodgkins disease (n=2) were treated on study. All pts had failed a median of 1 prior PBSCM (range 1-3) with chemotherapy followed by G-CSF(n=9) or G-CSF alone (n=6). Study treatment was neupogen 10ug/kg daily in the AM and AMD 3100 240ug/kg beginning day 4 at 2200. Apheresis of a 3 blood volume exchange began day five, 10 hours after the first AMD 3100 injection and 1 hour after the daily AM neupogen injection. This schedule continued daily until adequate CD34+ cells were collected or the pts were taken off study. Eleven (92%) pts mobilized adequate CD34+ cells to proceed with high dose chemotherapy and ASCT. A median of 2.1 million/kg CD34+ cells (range 1.1 to 5.5) were collected in a median of 3 (range 1-4) apheresis days. The maximum median peripheral blood CD34+ cell count prior to study was 8 cells/ul (range 1-25) but after administration of AMD3100 increased to 22 cells/ul (range 14-160) (p=0.03). Six pts reported mild reversible adverse events (AEs) possibly related to AMD3100, and no severe AEs were attributed to study drug. Nine pts proceeded to high dose chemotherapy and ASCT, 2 pts are pending start of ASCT, and one pt had insufficient CD34+ cells for ASCT. Eight pts are evaluable for engraftment with a median day to ANC greater than 500/ul of 12 days (range 11 to 15) and platelets greater than 20 K/ul of 20 days (range 14 to 39). There was no transplant related mortality at day 100 or unexpected transplant related toxicity. Two of 12 pts have died, both from relapsed disease 6 months post ASCT. A cohort of 60 pts underwent standard PBSCM and ASCT during the same time period as the study pts and the groups will be compared for differences in ASCT outcome and supportive care needs. In conclusion, this single institution case series of pts demonstrates that AMD3100 can mobilize significantly more CD34+ cells in pts who have failed standard PBSCM, with little toxicity and acceptable ASCT outcomes.

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EVALUATION OF SINGLE-DOSE PALIFERMIN TO REDUCE MUCOSITIS: ASSESSMENT OF EFFICACY AND SAFETY IN PATIENTS (PTS) WITH HEMATOLOGIC MALIGNANCIES (HM) RECEIVING AUTOLOGOUS PERIPHERAL BLOOD PROGENITOR CELL (PBPC) TRANSPLANTATION

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Palifermin has been approved for pts with HM undergoing PBPC transplantation with a regimen of 3 daily doses of 60 μg/kg pre- and post-myeloablative conditioning. The pre-dosing may, however, be inconvenient for some pts. This study was initially developed to demonstrate the non-inferiority of 3 collapsed (180 μg/kg) pre-dosing schedules in reducing the incidence of severe oral mucositis (OM) (WHO grade 3 or 4) induced by fractionated total body irradiation (fTBI) and high dose chemotherapy in pts with HM undergoing PBPC transplantation. The study was stopped early due to the decreased utilization of fTBI resulting in slow accrual. **Methods:** Pts were 18 to 74 years old with HM, a Karnofsky performance score ≥70%, and eligible for fTBI (12 Gy) followed by cyclophosphamide (100 mg/kg) and optional VP-16 (60 mg/kg), with autologous PBPC support. Pts were randomized (1:1:1:1) to receive the FDA approved palifermin dose and schedule of 60 μg/kg administered once daily for 3 days prior to the start of fTBI (control, Arm A) versus palifermin 180 μg/kg administered once only on day -1 (Arm B); day -2 (Arm C); or day -3 (Arm D) prior to the start of fTBI. Pts were stratified by VP-16 use and the number of days of fractionated TBI. All pts received palifermin 60 μg/kg for 3 days post transplant (days 0, 1, 2). **Results:** The incidence of severe OM has been previously reported for the 47 randomized pts (ASH 2006). The incidence of severe OM was 82% (9/11), 60% (6/10), 31% (4/13), and 75% (9/12) in Arms A, B, C and D, respectively. Most adverse events (AEs) occurred at frequencies < 10% and had a similar incidence across all treatment

arms. The most frequently observed AEs were diarrhea, nausea, vomiting, fatigue, and rash. The incidence of rash (40%, 36%, 46%, and 33% for Arms A, B, C, and D respectively) was comparable with the previously reported palifermin AE profile. Overall summary of AEs is presented in Table 1. **Conclusion:** The tolerability of the palifermin collapsed pre-dose arms is similar to Arm A, with an incidence of AEs across all arms that is consistent with the expected palifermin safety profile. These results suggest that a single pre-dose schedule can be tolerated and is a more convenient dosing schedule. Timing of palifermin in a collapsed dose administration regimen may affect the efficacy of OM reduction. This concept warrants further study.

Overall Summary of Adverse Events

	Arm A (N=10)	Arm B (N=11)	Arm C (N=13)	Arm D (N=12)
Pts who had any AEs	9(90%)	10(91%)	12(92%)	12(100%)
Pts who had study drug-related AEs	5(50%)	5(45%)	6(46%)	5 (42%)
Pts who had serious AEs	1(10%)	3(27%)	4(31%)	1 (8%)
Pts who had serious study drug-related AEs	0 (0%)	1 (9%)	0 (0%)	0 (0%)

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LOW DOSE AMBISOME ANTI-FUNGAL PROPHYLAXIS IN PEDIATRIC ALLOGENEIC UNRELATED HEMATOPOIETIC STEM CELL TRANSPLANT

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Invasive fungal infections (IFI) are a major cause of morbidity and mortality following allogeneic hematopoietic stem cell transplant (HSCT). To reduce the rate of IFI, in 1996 we initiated a program of bi-weekly lipid-based Amphotericin prophylaxis for patients receiving unrelated HSCT. A total of 76 consecutive patients received transplants from unrelated donors (Cord, MUD) between 1/1/1996 and 6/30/2005. Three patients with documented or suspected pre-HSCT IFI were excluded from analysis due to ongoing anti-fungal therapy at HSCT. Four patients received alternative prophylactic regimens by physician choice. An additional 3 patients were excluded due to death prior to initiation of anti-fungal prophylaxis. Thus, a total of 66 patients were deemed evaluable in this retrospective analysis. Sixty-four received Ambisome, 3mg/kg/dose twice weekly from day -1 thru day +100 post-HSCT. Two patients received bi-weekly Abelcet prophylaxis due to Ambisome allergy. Treatment was reduced or held for elevations of serum creatinine. Additional anti-fungal measures included HEPA air filtration, intranasal Amphotericin B, oral Clotrimazole and Nystatin. Median patient age at HSCT was 7.5 years (range, 0-24). Indications for HSCT included ALL (33), AML (13), CML (3), JMML (3), NHL (1), Aplastic Anemia (2), SCID (2), Metabolic Disorder (5), Other (4). The majority of patients had unrelated cord blood allografts (59) and received GVH prophylaxis which included ATG, cyclosporine and steroids. IFI documented by culture and/or histology during the prophylaxis period occurred in 9 of 66 evaluable patients (14%). Causative organisms were Aspergillus fumigatis (3), Aspergillus terreus (1), Candida parapsillosis (3), Candida tropicalis (1), Candida glabrata (1), Trichosporon (1). Sites of infection included blood (6), lung (4), other (2). Death due to IFI occurred in 3 of 66 patients (4%). Grade III renal toxicity occurred in 5 of 66 patients (8%); no grade IV renal toxicity was seen. We conclude that Ambisome anti-fungal prophylaxis is well tolerated and may reduce morbidity and mortality due to IFI in high risk HSCT patients.

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N-ACETYLCYSTEINE ADMINISTRATION FOR THE PREVENTION OF THE LIVER COMPLICATIONS FOLLOWING ALLOGENEIC HEMATAPOETIC STEM CELL TRANSPLANTATION

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Hepatic complications following allogeneic stem cell transplantation(HSCT) are a source of morbidity and mortality. A correlation exists between bilirubin levels(as a marker) and mortality and evidence exists that bilirubin itself may be responsible for end-organ damage. A study of >1400 HSCT patients found that an increase in bilirubin from 1mg to 3mg regardless of cause(GVHD, SOS, sepsis,etc.), was associated with a mortality hazards ratio=6.4. Mortality for bilirubin > 4mg was >50%.(Gooley et al. Hepatology 2005(41)345). Since correction of highly elevated bilirubin levels is seldom successful, early interventions are needed to prevent toxicity. N-acetylcysteine(NAC) is an anti-oxidant, useful at reducing stress from reactive oxygen species(ROS). Recipients of allogeneic HSCT at NMH were initiated on iv NAC 100mg/kg/d (4 daily doses). Criteria for use included 1) an increase in absolute bilirubin >2.0 or 2) doubling of baseline bilirubin > 1.6. All patients received ursodiol 300mg po tid. 31 patients who received NAC therapy for 7days and had complete laboratory data available were evaluated to determine the efficacy of NAC in preventing complications of liver disease following allogeneic HSCT. Conditioning regimens included.Busulfan /Fludarabine(n=15) Busulfan/Cytoxan(n=3), Cytoxan +/- Melphalan(n=9), TBI/VP-16(n=4).

Median day for initiation of NAC was 9 days post HSCT(range -4-43). Median bilirubin level prior to NAC therapy was 2.8mg(range1.6-13.7). Response: 24/31(77%)had positive responses(decreased from baseline), while in 7/31(23%) bilirubin increased during the 7days of treatment.(p=.001). Only 2/24 responders had GVHD, while 5/7 non-respoders had GVHD. (p=.0023:Fischers Exact test). Baseline bilirubin differed between responders and nonresponders(3.1 and 7.0 respectively:p=.0023). Responders improved liver toxicity grade(NCI criteria) from grade 3 to grade 2(median bilirubin improved from 2.8mg/dl to 1.7mg/dl). 4 responders whose bilirubin increased after NAC was discontinued, successfully responded after re-challenge. Overall 100day non-relapse mortality=22%: (Bu/Flu=3/15(20%):Bu/CY=0/3(0%): TBI/VP=3/4(75%):CY/Mel=1/9(11%).

NAC was effective in preventing the upward trend of bilirubin s/p HSCT, a complication associated with excess mortality. Initiating therapy before bilirubin levels become excessively elevated may improve successful outcomes. This preliminary data should encourage future research in prevention of liver toxicity post HSCT.

NAC therapy results

Conditioning regime	n	% responders (P)
Busulfan/Cytoxan	3	100
Busulfan/Fludarabine	15	80
TBI/VP-16	4	25
Cytoxan +/- Melphalan (non-myeloablative)	9	91
GVHD	7	28(.0023)
Bilirubin <3.1mg	24	72(.0023)
Bilirubin >7.0mg	7	28(.0023)